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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,659	04/11/2001	Adrian Whitty	00689-513 (A064 US)	2160
25181	7590	12/16/2003		
FOLEY HOAG, LLP PATENT GROUP, WORLD TRADE CENTER WEST 155 SEAPORT BLVD BOSTON, MA 02110			EXAMINER SEHARASEYON, JEGATHEESAN	
			ART UNIT 1647	PAPER NUMBER
DATE MAILED: 12/16/2003				

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/832,659

Applicant(s)

WHITTY ET AL.

Examiner

Jegatheesan Seharaseyon

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 March 2003 and 11 September 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-43 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 32-43 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 April 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
- a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6/27/03.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### DETAILED ACTION

1. This office action is in response to the amendment and response filed on 3/24/2003 and 9/11/2003. Claims 1-31 have been cancelled and claims 32-43 were added. Thus, claims 32-43 are pending.
2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.
3. Applicants change in the title is acknowledged.
4. The changes to figure legend are acknowledged.
5. Claim objection is withdrawn because Applicant has elected to cancel claim 6.

#### ***Claim Rejections - 35 USC § 112, first paragraph, withdrawn***

6. Applicant's amendments of 3/24/2003 have necessitated the withdrawal of the rejection of claims 1, 3, 6-10, 12, 15-18 and 28-31 under 35 USC § 112 1<sup>st</sup> paragraph for lack of written description.

#### ***Claim Rejections - 35 USC § 112, first paragraph, maintained***

7. Applicant's amendments of 3/24/2003 have necessitated the withdrawal of the rejection of claims 1, 3, 6-10, 12, 15-18 and 28-31 under 35 USC § 112 1<sup>st</sup> paragraph for lack of enablement with respect to mutant human IFN- $\beta$ 's or portion of the polypeptide. However, Applicant has not provided any evidence with respect to the activities of the various mutations. Thus, the rejection is maintained with respect to claims 32-43. Applicant has provided with activity information only for mutants C1 (SEQ ID NO: 51, D (SEQ ID NO: 56, DE1 (SEQ ID NO: 57), A1 (SEQ ID NO: 45), B2(SEQ ID NO: 51), CD2(SEQ ID NO: 55) in pages: 44 and 45. It is unclear if all the contemplated

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fusion proteins (SEQ ID: 45-60) have activity. As indicated in Paper NO: 13, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions and portions of the polypeptides are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made or portions generated with a reasonable expectation of success are limited. A large quantity of experimentation would have been necessary for the skilled artisan to generate the infinite number of mutant human IFN- $\beta$  fusion polypeptide recited in the claims and possibly screen the same for a useful activity. The specification fails to provide sufficient direction/guidance regarding which structural features are required in order to provide the mutant human IFN- $\beta$  fusion polypeptide with activity. The state of the prior art establishes the unpredictability of the effects of mutation on protein structure and function. Finally, the breadth of the claims is large, failing to recite any structural or functional limitations for the recited mutant human IFN- $\beta$  fusion polypeptides. For all of these reasons, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. Therefore, rejection under lack of enablement is maintained.

***Claim Rejections - 35 USC § 112, second paragraph, withdrawn***

8. The rejection of claims 1, 3, 6-10, 12, 15-18 and 28-31 under 35 USC § 112 2<sup>nd</sup> paragraph for being vague and indefinite is withdrawn in view of Applicants arguments of 3/24/2003.

***Claim Rejections - 35 USC § 103, maintained***

8. Claims 32-37 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Chang et al. (U. S. Patent No. 5,908,626) and Bell et al. (U. S. Patent No. 4,914,033) in view of Carpon et al. (U. S. Patent No. 5,116,964) and Katre et al. (U. S. Patent No. 4,766,106) for reasons stated in Paper No: 13 for previously pending claims 1-18, 23-25 and 28-31. Applicant's arguments filed on 3/24/03 have been fully considered but are not persuasive.

Applicant points to several alleged deficiencies present in Chang et al. such as the presence of hinge region, CH2 and CH3 domains. However, these issues are addressed by the combination of references. Thus, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Furthermore, Applicant alleges that Chang et al. teaches away from hybrid recombinant proteins lacking a peptide linker and that instant claims does not recite a peptide linker. Chang teaches methods to designing INF $\beta$ -Fc hybrids to over come the problem of hybrid peptides being neoantigens and which are immunogenic (column 1, lines 55-57). In addition, the instant

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claims are drawn to a polypeptide comprising the amino acid sequence of SEQ ID NO: 60; and a hinge, CH2 and CH3 domain of an immunoglobulin which does not preclude a linker. Thus, Chang et al. teachings meet the limitations of instant claim 32.

Applicant alleges that Bell, Capon and Katre references do not cure the perceived deficiencies of Chang reference by attacking the references individually. However, as indicated above, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. Therefore, the instant invention is obvious over Chang et al. (U. S. Patent No. 5,908,626) and Bell et al. (U. S. Patent No. 4,914,033) in view of Carpon et al. (U. S. Patent No. 5,116,964) and Katre et al. (U. S. Patent No. 4,766,106).

9. No claims are allowable.

**10. THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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### **Contact Information**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS

A handwritten signature in cursive script that reads "Lorraine Spector". The signature is written in black ink and is positioned above the printed name and title.

**LORRAINE SPECTOR  
PRIMARY EXAMINER**